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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,871	05/09/2001	C. Frank Bennett	ISPH-0543	4942

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,871	BENNETT ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Arguments

1. Claims 1, 6, and 8-10 remain rejected under 35 U.S.C. 102(e) as being anticipated by Stinchcomb et al. (US 5,877,021; '021); Claims 1-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Stinchcomb et al. (US Pat. No. 5,877,021) or Freeman et al. (US Pat. No. 5,942,607), either in view of Abramowicz et al. (WO 94/17773) and Cooper et al. (WO 93/24134 A1) for the reasons of record in the Office Action mailed 4-10-03.

Applicant's arguments filed 7-14-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the '021 patent disclosure mentions antisense nucleic acid molecules only in passing (see e.g., col. 5, line 66, to col. 6, line 6; col. 6, line 39-44) and distinguishes molecules of this type from ribozymes in that antisense molecules are expressly defined as being "non-enzymatic." (Col. 6, line 39-40). Beyond this disclosure, the '021 patent specification is completely silent with respect to the invention recited in the presently rejected claims.

Contrary to Applicants assertions, Stinchcomb et al., in the summary of the invention, clearly state that their disclosed invention is drawn to novel nucleic acid-based techniques, which include for example, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, 2-5A antisense chimeras, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups, and methods for their use to induce graft tolerance, to treat autoimmune diseases such as lupus, rheumatoid arthritis, multiple sclerosis and to treatment of allergies. Moreover, Stinchcomb et al. clearly state that the nucleic acid-based techniques are directed to inhibiting the synthesis of B7-1, B7-2, B7-3 and CD40 proteins.

In a preferred embodiment, Stinchcomb et al. teach a method for the treatment of autoimmune diseases, inflammatory disorders and allergies by inhibition of B7-1, B7-2, B7-3, and CD40 (see col. 1, lines 12-15). In one specific embodiment autoimmune diseases include, for example, "psoriasis." (see col. 5, lines 15-20).

Stinchcomb et al. specifically disclose hammerhead ribozymes targeted to the B7-1 and B7-2 transcripts (see example 1, starting col. 13, line 41), wherein the typical hammerhead ribozyme is approximately 13 to 40 nucleotides in length (note Table I at col. 15, lines 36-37) and discloses a number of potential target sequences for hammerhead ribozymes within the human B7-1 and B7-2 transcripts (Tables II and VI). It is noted that the instant claims are directed to antisense sense compounds, one of skill in the art would immediately recognize that ribozymes are a form of antisense compound since it hybridizes to the target nucleic acid in an antisense manner.

Additionally, Applicants argue that the cited reference do not teach topical administration. Contrary to Applicant's assertion, as stated in the prior Office Action, administration of the compositions of the Stinchcomb et al. invention may include, among others, ***topical*** (col. 12, lines 18-36). Stinchcomb et al. further teach that the compounds of the invention may be delivered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres.

It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure.

As stated in the prior Office Action, absent evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the teachings of Stinchcomb et al. and Freeman et al. to make the instantly claimed invention, *specifically* wherein said invention comprises a method for treating inflammatory skin disorders such as dermatitis and eczema, and wherein the method comprises topically applying an antisense compound 8 to 30 nucleobases in length comprising the base, sugar, covalent linkage, and lipophilic modifications taught by Cooper et al. Additionally, it would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Freeman or Stinchcomb et al. to make a pharmaceutical composition comprising an immunosuppressive agent, oligonucleotide inhibitors of human B7-1 and B7-2 expression, and a carrier. One of ordinary skill in the art would have been motivated to modify the antisense oligonucleotides of Freeman et al. (or the antisense nucleic acid of Stinchcomb et al.) with the sugar, base, the internucleosidyl backbone modifications, and lipophilic agents of Cooper et al. since these modifications are disclosed as enhancing the cellular properties of oligomeric compounds comprising these modifications. Furthermore, the disclosure of Cooper et al. also provides motivation and an expectation of success for the use of modified antisense oligonucleotides of 8 to 40 nucleotides in length for the treatment of various inflammatory skin disorders including dermatitis and psoriasis. One of ordinary skill in the art would have been motivated to modify the methods of Stinchcomb et al. and Freeman et al. to comprise the treatment of conditions such as atopic dermatitis, and eczema since the prior art (Abramowicz et al.) discloses that these conditions can be treated by administration of an inhibitor of B7 expression.

One of ordinary skill in the art would have been motivated to design a pharmaceutical composition comprising oligonucleotide inhibitors of ICAM-1 (i.e. an anti-inflammatory or immunosuppressive agent, see claim 13), B7-1, and B7-2 for the treatment of an inflammatory skin disorder, since the prior art clearly discloses that inhibitors of ICAM-1 and B7 activity would be useful in the treatment of inflammatory skin diseases such as atopic dermatitis and eczema (Abramowicz et al.). Additionally, Stinchcomb et al. describes the use of immunosuppressive agents such as cyclosporine, azathioprine, and anti-B7 antibodies for the treatment of allograft rejection (col. 3, lines 25-68), therefore these compounds are disclosed in the prior art as having similar functions.

Moreover, one of ordinary skill in the art would have been motivated to make a composition comprising an anti-inflammatory or immunosuppressive agent and inhibitors of B7 activity since they are disclosed in the prior art as comprising similar functional properties, particularly for the treatment of allograft rejection (Stinchcomb), and for use in the treatment of an inflammatory skin disorder as per the teachings of Abramowicz. Furthermore, as per MPEP § 2144.06 "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose." "[T]he idea of combining them flows logically from their having been individually taught in the prior art." MPEP § 2144.06.

Conclusion

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 9:00AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
September 30, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635